Abstract

Charles University

Faculty of Pharmacy in Hradec Králové

Department of Biochemical Sciences

Candidate: Mgr. Kateřina Lojdová

Supervisor: RNDr. Eva Novotná, Ph.D.

Consultant: RNDr. Lucie Zemanová, Ph.D.

Title of thesis: Inhibitors of human enzyme AKR1C3 of plant origin

Enzyme AKR1C3 is a part of large superfamily of aldo-keto reductases. It is a hydroxysteriod dehydrogenase, in human body it participates among others in steroid hormone metabolism but also in activation and deactivation of some drugs. Increased expression of this enzyme is linked to higher aggressivity of some neoplastic diseases and poor prognosis of the treatment, e.g. prostate cancer. This makes AKR1C3 an interesting target for farmaceutical and medical research. Discovery of strong and selective AKR1C3 inhibitor is the first step in finding a drug, that could affect tumor metabolism and restore its sensitivity to treatment.

There were 32 naturally occuring compounds from flavonoid and alkaloid groups tested in this study. Its goal was to determine inhibiton efficacy of selected compounds to enzyme AKR1C3. Reduction of a potential anticancer drug oracin to dihydrooracin was used for the measurement, the results were evaluated using an HPLC analysis. IC_{50} was determined for compounds with significant inhibitory effect.